34. (Amended) A vector according to claim 31, wherein the polypeptide consists of SEQ ID NO:2.

35. (Amended) A recombinant expression vector comprising a promoter operably linked to an expressed polynucleotide which encodes a polypeptide and hybridizes under highly stringent conditions to a nucleic acid consisting of SEQ ID NO:3, wherein said polypeptide mediates the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein and said highly stringent conditions comprise hybridization and wash conditions selected to be 5° C lower than the thermal melting point (Tm) for said nucleic acid at a defined ionic strength and pH.

E1 Cont

36. (Amended) A vector according to claim 35, wherein the polypeptide comprises SEQ ID NO:4 or conservatively modified SEQ ID NO:4. D

37. (Amended) A vector according to claim 35, wherein the polypeptide comprises SEQ ID NO:4.

38. (Amended) A vector according to claim 35, wherein the polypeptide consists of SEQ ID NO:4.

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39. (Unamended) A recombinant cell transduced with the vector of claim 31.

40. (Unamended) A recombinant cell transduced with the vector of claim 32.

41. (Unamended) A recombinant cell transduced with the vector of claim 33.

42. (Unamended) A recombinant cell transduced with the vector of claim 34.

43. (Unamended) A recombinant cell transduced with the vector of claim 35.

44. (Unamended) A recombinant cell transduced with the vector of claim 36.

45. (Unamended) A recombinant cell transduced with the vector of claim 37.

46. (Unamended) A recombinant cell transduced with the vector of claim 38.

REMARKS

Amendments

Claims 31 and 35 have been amended to emphasize that the expressed polynucleotide encodes a CAAX protease. Dependent claims 32-34 and 36-38 are amended to further restrict the expressed polypeptide in terms of SEQ ID NOS:2 and 4, respectively. These amendments introduce no new matter.

Finality

The Action provides a new art rejection. Contrary to the false and unsupported representation of the Action, this rejection was not necessitated by any amendments to our claims. Specifically, the cited Lye reference is cited against claims 35-38 and 43-46 as teaching a composition identical to our SEQ ID NO:3 and encoding our SEQ ID NO:4. This same subject matter was recited in claims 10-12 prior to our amendment. Furthermore, a new enablement rejection is applied to claims 31-33 as directed to vectors which, inter alia, hybridize with SEQ ID NO:2. This same subject matter was recited in claim 13 prior to our amendment. Accordingly, the finality of this rejection is improper.

35USC131

The present Office Action is the second examination on the merits of this application raising new issues. This Action exceeds the Commissioner's authority to subject Applicants to "an examination" (not multiple, piecemeal examinations) under 35USC131. See also, 37CFR1.104(b) which provides that an Examiner's Action "will be complete as to all matters." On this basis, we submit that the Commissioner has exhausted statutory authority to further reject this application, and on this basis alone we request immediate allowance of the application.

35USC112, first paragraph (enablement)

The Action acknowledges that the specification enables a vector comprising a

polynucleotide which hybridizes to a nucleic acid which encodes SEQ ID NO:2 and wherein the polypeptide is a CAXX protease; Action, p.2, lines 11-15). As the amended claims are within this scope, they avoid this rejection.

35USC112, first paragraph (written description)

As amended, the claims are limited so that the polynucleotide encodes a polypeptide with recited CAAX proteolytic activity; Action, p.7, lines 18-20. Hence, the amended claims avoid this rejection.

35USC112, second paragraph

All the pending claims expressly recite that the highly stringent conditions comprise hybridization and wash conditions selected to be 5° C lower than the thermal melting point (Tm) for said nucleic acid at a defined ionic strength and pH. It is well-known in the art that the T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe; Specification, p.8, lines 15-19. The allegation that the recited highly stringent conditions are indefinite is unsupported.

35USC103(a)

The art rejection applied to claims 31-34 and 39-42 (reciting SEQ ID NOS:1 and 2) relies on Rose, M. et al. (GenBank Database, Accession No. Z49617), which is dated Aug 11, 1997, more than a year after our Aug 7, 1996 priority date, and is hence not prior art. The examiner has hand-written on the NCBI printout "Public Availability: 10/6/95". Upon telephone inquiry, the Examiner indicated that the only support for his hand-written comment was a "creation-date" annotation associated with the GenBank entry. However, the same annotation continues that the entry was updated on Aug 11, 1997. The Examiner indicated that the Action is premised on an assumption that the relied upon sequence was published on Oct 6, 1995. Such an assumption goes farther than relying on manuscript submission dates instead of publication dates - a practice disclaimed by the Office - for with the latter, there is no assurance that the information was modified at all. Here, the evidence dictates that the entry purportedly created on Aug 11, 1997 is not the same as that created on Oct 6, 1995. The Action offers no evidence that the relied upon sequence was presented to GenBank or created or published at any time prior to Aug 11, 1997.

The Examiner apparently seeks to shift the burden to Applicants to prove that Rose et al. is not prior art. We believe this position untenable as imposing an inherently impossible proof on the Applicants, and misconstruing the duty of the Examiner, which is to allow our claims unless he can establish a prima facie case of non-patentability, which includes showing that the cited art is prior art. Here, the uncontroverted evidence unequivocally demonstrates that what is cited was not what was publically available as of Oct 6, 1995.

In any event, the entire yeast genome had been largely sequenced prior to the filing of our patent application, including the identification of thousands of ORFs which were not even known to encode functional mRNA. Even if these ORFs contained an identical or substantially identical sequence, the claimed compositions would be neither anticipated nor obvious. First, even if a yeast chromosome sequence is determined (and it appears that a sequence encoding Afc1p (SEQ ID NO:2) is found on the yeast X chromosome), our claims do not encompass any chromosome. Second, our claims require that the coding sequence be operatively joined to a promoter. In the absence of any evidence for function, there would be no motivation to select out one of the thousands of yeast ORFs of unknown function, isolate what may or may not be a coding sequence, and operatively join it to a promoter.

The art rejection applied to claims 35-38 and 43-46 (reciting SEQ ID NOS:3 and 4) relies on Lye, et al. (GenBank Database, Accession No. Z49260), which is also dated Aug 11, 1997, more than a year after our Aug 7, 1996 priority date, and is hence not prior art. Instead of a publication date, the Examiner appears to rely on a purported unpublished submission date. This is improper; if a database entry does not recite a publication date, it can not be relied upon as prior art; see MPEP2128. The Action offers no evidence that the relied upon sequence was published at any time prior to Aug 11, 1997.

In any event, the entire yeast genome had been largely sequenced prior to the filing of our patent application, including the identification of thousands of ORFs which were not even known to encode functional mRNA. What Lye discloses are computer predictions of thousands of possible CDS regions. A computer is programmed to input raw genomic sequence, select all possible CDS regions over 100 codons, and then exclude those that are more than 50% overlapped by a larger predicted CDS. The authors promise that CDS regions of the initial dataset subsequently eliminated by the algorithm are nevertheless "available upon request." In addition, the disclosure provides algorithm-predicted PROSITE database matches, though the

authors caution that some of these may be "fortuitous".

Lye does not disclose any gene or gene product, but the results of a first run effort to sequence the entire XIII chromosome of Saccharomyces cerevisiae. That natural yeast XIII chromosome is, of course, prior art, and Lye provides no more than an inherent property of that chromosome - its sequence. Lye discloses no more than raw genomic data weighted by a computer for thousands of possible genes and genetic elements. The Examiner uses our own disclosure to select out one of these and uses our own disclosure to provide motivation to recombine it in an expression vector. In the absence of any evidence for function, there would be no motivation to select out one of the thousands of yeast ORFs of unknown function, isolate what may or may not be a coding sequence, and operatively join it to a promoter in an expression vector, as expressly required by our claims.

Absent a prior art suggestion that SEQ ID NO:1 or 3 encodes a protein of determined function sufficient to motivate the isolation, cloning and expression of such SEQ ID NO using techniques such as those of the cited Nozaki et al. (US Pat No 4,997,767) and Sambrook, J. et al. (Mol. Cloning, Cold Spring Harbor Press, p. 16.3-16.16) references, the claims are in compliance with 35USC102 and 103.

The Examiner is invited to call the undersigned if he would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

Applicants confirm their request made in a telephone conference with SPE Achutamurthy to discuss the prosecution of this and copending Application Serial Nos. 09/184,964 and 09/167,132 and solicit from the Examiner a telephone call indicating a time he and his supervisor will be available.

Applicants hereby petition for any necessary extension of time pursuant to 37 CFR 1.136(a). The Commissioner is hereby authorized to charge any fees or credit any overcharges relating to this communication to our Deposit Account No. 19-0750 (order no. B96-021-3).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP

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